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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/689,539	10/21/2003	David Burrell	65042-014	9328

7590 07/16/2007

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EXAMINER	
SPIVACK, PHYLLIS G	
ART UNIT	**PAPER NUMBER**
1614	

MAIL DATE	DELIVERY MODE
07/16/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/689,539	BURRELL, DAVID	
	Examiner	Art Unit	
	Phyllis G. Spivack	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3-22-04;10-4-04;12-29-04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's Response filed February 27, 2007 to the Election of Species Requirement mailed January 8, 2007 is acknowledged. Applicant has elected with traverse simethicone as an antiflatulent, diphenhydramine as a histamine antagonist, Larch arabinogalactans as a prebiotic and *Bifidobacterium infantis* as a probiotic.

The traversal is on the grounds that there is no serious burden presented to the Examiner to examine all of the claims in a single application because in Applicant's view, the recited species are different embodiments of the same invention.

The present claims broadly claim any antiflatuent, any competitive reversible histamine H_1-receptor antagonist, any prebiotic and any probiotic in any number of combinations. Further, the present claims are drawn to a plethora of unrelated pathologies involving different organ systems and unknown etiologies. The claims are unduly broad and clearly present an undue search burden to the Examiner.

Applicant's argument has been given careful consideration but is not found persuasive.

The Elections of Species Requirement are still deemed proper and are adhered to. The Requirements are hereby made FINAL.

Accordingly, the subject matter initially under consideration are those compositions and methods of treatment drawn to gastrointestinal disorders and treatment of colic comprising administering simethicone as an antiflatulent, diphenhydramine as a histamine antagonist, Larch arabinogalactans as a prebiotic and *Bifidobacterium infantis* as a probiotic, claims 1-41.

Those pharmaceutical compositions and methods comprising administering other antiflatulents, histamine antagonists, prebiotics and probiotics, other than those recited *supra*, are presently withdrawn from consideration by the Examiner, as drawn to non-elected inventions, 37 CFR 1.142(b). Re-affirmation of the elections is requested when Applicant responds to this Office Action.

Information Disclosure Statements (IDS) filed March 22, 2004, October 4, 2004 and December 29, 2004 are further acknowledged and have been reviewed to the extent each is presented in the English language. All of the cited references in the IDS filed October 4, 2004 are encompassed in the December 29, 2004 filing.

The disclosure is objected to for the following informalities: "Diphenhydramine" is incorrectly spelled in claims 13 and 33.

Appropriate correction is required.

Claim 4 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim, or amend the claim to place the claim in proper dependent form, or rewrite the claim in independent form. Intended use confers no patentable weight to composition claims. *In re Hack*, 114 USPQ 161.

Applicant is advised that should claim 1 be found allowable, claim 7 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof.

Claim 1 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 7. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is

proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claims 4 and 6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

The term "including" in claims 4 and 6 renders the claims indefinite. It is unclear whether or not a claim limitation is intended.

Claims 5, 6 and 27-41 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention. The claims are broadly directed to the treatment of numerous gastrointestinal disorders and unrelated diseases of other organ systems such as lymphoma, syphilis, sarcoidosis, tuberculosis, motion sickness and otitis media. The specification provides support for treatment of colic comprising administering simethicone and diphenhydramine. The disclosed pharmaceutical compositions, Examples 1-8, pages 20-30 in the specification, are limited to the single antiflatulent simethicone and the single competitive reversible histamine H_1-receptor antagonist diphenhydramine for treatment of colic and any gastrointestinal disorder.

Attention is directed to *In re Wands*, 8 USPQ2d 1400 where the court set forth factors to consider when assessing whether or not a disclosure would require undue experimentation. These factors are:

1) the quantity of experimentation necessary

2) the amount of direction or guidance provided

3) the presence or absence of working examples

4) the nature of the invention

5) the state of the art

6) the relative skill of those in the art

7) the predictability of the art and

8) the breadth of the claims.

The instant specification fails to provide guidance that would allow the skilled artisan background sufficient to practice the instant invention without resorting to undue experimentation in view of further discussion below.

The nature of the invention, state of the prior art, relative skill of those in the art and the predictability of the art

The claimed invention relates to therapeutic modalities for gastrointestinal pathologies. Each of the disclosed compositions in Examples 1-9, pages 20-30 in the specification, are limited to only diphenhydramine as a competitive reversible histamine H_1-receptor antagonist and simethicone as an antiflatulent. The intended use is stated to be relief from pain and/or gastrointestinal discomfort.

The relative skill of those in the art is generally that of a Ph.D. or M.D. with expertise in the area of gastroenterology.

The breadth of the claims

The claims are very broad in terms of the structurally diverse compounds encompassed in the language of the claims and the hypothetical application to any

gastrointestinal disorder, including colic. Colic refers to paroxysms of pain and associated crying and irritability in young infants, due to causes such as swallowing air, emotional upset or overfeeding. The index entitled **Gastrointestinal Disorder** from The Merck Index is provided to show the breadth of pathologies encompassed in instant claims 5 and 6. Further, a description of **Colic** is provided to show the unpredictable nature of the condition.

The amount of direction or guidance provided and the presence or absence of working examples

The working examples are limited to the administration of diphenhydramine and simethicone, optionally with larch arabinogalactans and/or *Bifidobacterium infantis*. Examples 1-8 disclose pharmaceutical compositions comprising simethicone, as an antiflatulent, diphenhydramine, as a histamine antagonist, optionally, Larch arabinogalactans as a prebiotic, and/or various probiotics including *Bifidobacterium infantis*. In Example 9, page 30, parents of an infant suffering from colic provide testimony that the infant responded favorably to administration of simethicone substantially together with diphenhydramine.

The quantity of experimentation necessary

Applicants have failed to provide guidance as to which particular compounds among the recited antihistamines, antiflatulents, probiotics and prebiotics would be preferred for each particular disease state. No dosing regimens with respect to modes of administration or timing are disclosed that would appropriately relate to the plethora of diseases encompassed in the claim language.

Examples 1-8 in the specification merely prophesize that such administration provides relief from pain and/or gastrointestinal discomfort.

However, *Genetech Inc. vs. Nova Nordisk* states, "[A] patent is not a hunting license. It is not a reward for a search but a compensation for its successful conclusion and 'patent protection' is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" (42 USPQ 2d 1001, Fed. Circuit, 1997).

The skilled artisan would expect the interaction of a particular combination of agents in a therapeutic regimen to be very specific and highly unpredictable absent a clear understanding of the structural and biochemical basis for each agent. The instant specification sets forth no such understanding. An efficacious effect in treating heartburn does not presage efficacy for treating irritable bowel syndrome. Absent reasonable *a priori* expectations of success for using any particular combination of agents for the plethora of disease states encompassed in the claim language, one skilled in the gastroenterology art would have to test extensively many compounds/prebiotics/probiotics, and combinations thereof, to discover which prove efficacious. Since each prospective embodiment, as well as future embodiments as the art progresses, would have to be empirically tested, undue experimentation would be required to practice the invention as it is claimed in its current scope. The specification provides inadequate guidance to do otherwise.

Considering the state of the art, which does not recognize across-the-board treatment for any and all gastrointestinal disorders, a high degree of unpredictability in treating any gastrointestinal disorders and the lack of guidance provided by the specification, one of ordinary skill in the gastroenterology art would be burdened with undue experimentation.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-41 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. In the instant case, the claims disclose pharmaceutical compositions comprising simethicone and diphenhydramine, optionally with larch arabinogalactans and/or *Bifidobacterium infantis,* among other probiotics. There is insufficient written basis commensurate in scope with the subject matter of claims 1-41. This is a Written Description rejection.

M.P.E.P. § 2163 states, "An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such

descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention...one must define a compound by 'whatever characteristics sufficiently distinguish it'. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process."

Examples 1-9 are disclosed on pages 20-30 of the specification drawn exclusively to diphenhydramine and simethicone. However, Applicant has not conveyed possession of the invention with reasonable clarity to one skilled in the art, particularly with respect to formulations comprising other histamine H_1-receptor antagonists or antiflatulents. The disclosure lacks sufficient written description for all claimed limitations. No working examples are provided that would describe to one of ordinary skill in the art an embodiment that meets all the limitations of the claims. Sufficient guidance to support predictable operability of the invention to one of ordinary skill in the art is absent.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sims et al., WO 95/01792, and Paul et al., U.S. Patent 6,241,983.

Sims teaches the administration of the anti-flatulent simethicone with the antihistamine diphenhydramine to treat gastrointestinal disorders that may result from overindulgence. See claim 11 on page 21. Diphenhydramine is formulated at amounts ranging from 12.5mg to 50 mg. See the Examples. See page 14 where simethicone is formulated in a typical dosage range of 20-40 mg to provide antiflatulent relief. The open language of the present claims allows for the inclusion of any number of additional active or inactive agents. Paul teaches the administration of both *Bifidobacterium* species and larch arabinogalactans to maintain gastrointestinal health. See column 5, lines 22-37, *inter alia*, column 9, lines 34-39, and claims 31 and 41.

In view of the teachings of Sims and Paul, one skilled in the gastroenterology art would have been motivated to prepare formulations comprising diphenhydramine and simethicone, optionally with larch arabinogalactans and/or *Bifidobacterium infantis, or* other probiotics. Such would have been obvious in the absence of evidence to the contrary because in the cases of overindulgence in an adult or overfeeding an infant, both simethicone and diphenhydramine have been efficaciously administered. Paul teaches beneficial effects following the administration of bifidobacteria on gastrointestinal health. These bacteria lower the intestinal pH, thereby inhibiting overgrowth of gastrointestinal pathogens. Further, larch arabinogalactans provide dietary fiber to improve bowel function.

With respect to optimal dosing regimens and optimal dose ranges of the active agents in the instant compositions and methods of use, it is not inventive to discover the optimum or workable ranges by routine experimentation when general conditions of a

claim are disclosed in the prior art. See *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233,235 (CCPA 1955) and MPEP 2144.05(II). The determination of the optimum dosage regimen to employ with the presently claimed active agents would have been a matter well within the purview of one of ordinary skill in the art. Such determination would have been made in accordance with a variety of factors. These would have included such factors as the age, weight, sex, diet and medical condition of the patient, severity of the disease, the route of administration, pharmacological considerations, such as the activity, efficacy, pharmacokinetics and toxicology profiles of the particular compound employed, whether a drug delivery system is utilized and whether the compound is administered a part of a drug combination. Thus, in the absence of evidence to the contrary, the currently claimed specific dosage amounts and dosage regimens are not seen to be inconsistent with the dosages that would have been determined by the skilled artisan.

No claim is allowed.

Fusch et al., Pediatrika, is cited to show further the state of the art with respect to the safe and effective administration of prebiotics and probiotics to infants.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Phyllis G. Spivack whose telephone number is 571-272-0585. The Examiner can normally be reached on 10:30 AM-7 PM.

If attempts to reach the Examiner by telephone are unsuccessful after one business day, the Examiner's supervisor, Ardin Marschel, can be reached on 591-272-

0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phyllis Spivack

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PHYLLIS SPIVACK
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July 7, 2007